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AGGCTGTCCCACCCACCATCTGCACCCGCTGCAGCGCCCGCGCCCCTGTCCCGCGCCGTAGTCGTCATTTGTAGCCC
GCCTGCCGCTCCCGGGGACCCGATCCTACCCTGGGTGCGGGGCAGAGCGGGCATGGCCCGTCTGGGGACCGCCTGCC
CTGCGCTGGCGCTGGCCCTGGCACTTGTGGCGGTGGCCCTGGCTGGAGTCAGAGCCCAGGGCGCAGCCTTCGAGGAG
CCTGACTATTACAGCCAGGAGCTCTGGCGGCGCGGGCGCTATTATGGGCATCCGGAGCCTGAGCCGGAGCCGGAGCT
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CTCCCAAGAAGGCCATCAAGCCCAAGAAGGCTCCCAAGAGGGAGAAGTTAGTTGCAGAGACGCCTCCACCAGGTAAA
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CATCGAAGCGTTATGGCCTGGGAGCCCACCGGGGGAGACTCAACATCCAGGCAGGCATTAATGAAAATGACTTTTAC
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AGGGGTCATTACCCAAGGAAGGAACTCTCTCTGGCTGAGTGACTGGGTGACATCCTATAAAGTCATGGTGAGCAATG
ACAGCCACACATGGGTTACTGTGAAGAATGGATCTGGCGACATGATATTTGAAGGAAACAGTGAGAAGGAGATTCCT
GTGCTCAATGAGCTGCCAGTCCCCATGGTGGCCCGCTACATTCGCATAAACCCTCAGTCCTGGTTTGATAACGGGAG
CATCTGCATGAGGATGGAGATCTTGGGCTGCCCACTGCCGGATCCTAATAACTATTATCACCGACGTAATGAGATGA
CCACCACGGATGACCTGGATTTTAAGCACCACAACTATAAGGAAATGCGCCAGTTGATGAAGGTTGTCAATGAAATG
TGCCCCAATATTACCAGGATTTACAACATTGGCAAAAGCCACCAGGGCCTGAAATTGTATGCGGTAGAGATCTCTGA
CCATCCTGGGGAACATGAAGTTGGTGAGCCCGAGTTCCACTACATCGCAGGGGCCCACGGCAATGAGGTTCTGGGAC
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GGGAGGCTGGTCCCTGGGACGTTGGACCCATGATGGCATCGATATCAACAACAACTTTCCGGATTTAAACTCGCTGC
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TCTGAGAATGCCACAGTGGCCACAGAGACCAGAGCCGTCATCGCCTGGATGGAGAAGATCCCGTTTGTGCTGGGAGG
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CCCCAACACCTGATGATCATGTGTTCCGCTGGCTGGCGTATTCCTACGCCTCCACTCACCGCCTCATGACAGATGCC
AGGAGGCGAGTGTGCCACACGGAAGATTTTCAGAAGGAGGAGGGCACCGTCAATGGGGCTTCCTGGCACACAGTGGC
TGGAAGTCTAAACGATTTCAGCTACCTCCATACAAACTGCTTTGAGCTGTCCATCTACGTGGGCTGTGATAAATACC
CACACGAGAGCGAGCTGCCGGAGGAATGGGAGAATAACCGGGAGTCTCTGATTGTGTTCATGGAGCAGGTTCATCGA
GGCATCAAAGGCATAGTGAGAGATTTACAAGGGAAAGGGATTTCAAATGCTGTCATCTCTGTGGAAGGTGTTAACCA
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AAGACCAACCTGGCTAGGATAAGAGAAATTATGGAGACATTTGGGAAGCAGCCTGTCAGCCTACCCTCCAGGCGCCT
GAAGCTGCGGGGACGGAAAAGGCGGCAGCGTGGGTGACCCTGTCGGACACTTGAGACATACCCCAGACCGTGCAAAT
AAAAATCCACTCCAGTAGTAAAAAAA
(SEQ ID NO:1)

MARLGTACPALALALALVAVALAGVRAQGAAFEEPDYYSQELWRRGRYYGHPEPEPEPELFSPSMHEDLR
VEEQEQQEPHQQGHRTPKKAIKPKKAPKREKLVAETPPPGKNSNRKGRRSKNLEKAASDDHGVPVAHEDV
RESCPPLGLETLKITDFQLHASTSKRYGLGAHRGRLNIQAGINENDFYDGAWCAGRNDLHQWIEVDARRL
TKFTGVITQGRNSLWLSDWVTSYKVMVSNDSHTWVTVKNGSGDMIFEGNSEKEIPVLNELPVPMVARYIR
INPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTTTDDLDFKHHNYKEMRQLMKVVNEMCPNITRIY
NIGKSHQGLKLYAVEISDHPGEHEVGEPEFHYIAGAHGNEVLGRELLLLLLHFLCQEYSAQNARIVRLVE
ETRIHILPSLNPDGYEKAYEGGSELGGWSLGRWTHDGIDINNNFPDLNSLLWEAEDQQNAPRKVPNHYIA
IPEWFLSENATVATETRAVIAWMEKIPFVLGGNLQGGELVVAYPYDMVRSLWKTQEHTPTPDDHVFRWLA
YSYASTHRLMTDARRRVCHTEDFQKEEGTVNGASWHTVAGSLNDFSYLHTNCFELSIYVGCDKYPHESEL
PEEWENNRESLIVFMEQVHRGIKGIVRDLQGKGISNAVISVEGVNHDIRTASDGDYWRLLNPGEYVVTAK
AEGFITSTKNCMVGYDMGATRCDFTLTKTNLARIREIMETFGKQPVSLPSRRLKLRGRKRRQRG (SEQ
ID NO:2)

FIGURE 1

APPROVED O.G. FIG.
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underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

[AGGCTGTCCCACCCACCATCTGCACCCGCTGCAGCGCCCGCGCCCCTGTCCCGCGCCGT
AGTCGTCATTTGTAGCCCGCCTGCCGCTCCCGGGGACCCGATCCTACCCTGGGTGCGGGG
CAGAGCGGGCATGGCCCGTCTGGGGACCGCCTGCCCTGCGCTGGCGCTGGCCCTGGCACT
TGTGGCGGTGGCCCTGGCTGGAGTCAGAGCCCAGGGCGCAGCCTTCGAGGAGCCTGACTA
TTACAGCCAGGAGCTCTGGCGGCGCGGGCGCTATTATGGGCATCCGGAGCCTGAGCCGGA
GCCGGAGCTCTTCTCGCCTTCAATGCA]TGAAGACCTTAGGGTGGAGGAGCAGGAACAGC
AGGAGCCGCACCAGCAGGGCCACAGAACTCCCAAGAAGGCCATCAAGCCCAAGAAGGCTC
CCAA[GAGGGAGAAGTTAGTTGCAGAGACGCCTCCACCAG]GTAAAAATAGCAACAGAAA
AGGCAGAAGAAGCAAGAATCTTGAGAAAGCTGCCAGTGATGACCATGGTGTCCCTGTGGC
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CTTCCAGCTGCATGCCTCCACATCGAAGCGTTATGGCCTGGGAGCCCACCGGGGGAGACT
CAACATCCAGGCAGGCATTAATGAAAATGACTTTTACGATGGGGCTTGGTGTGCTGGTAG
GAACGACTTGCATCAGTGGATCGAAGTGGATGCCCGGCGCCTGACCAAGTTCACAGGGGT
CATTACCCAAGGAAGGAACTCTCTCTGGCTGAGTGACTGGGTGACATCCTATAAAGTCAT
GGTGAGCAATGACAGCCACACATGGGTTACTGTGAAGAATGGATCTGGCGACATGATATT
TGAAGGAAACAGTGAGAAGGAGATTCCTGTGCTCAATGAGCTGCCAGTCCCCATGGTGGC
CCGCTACATTCGCATAAACCCTCAGTCCTGGTTTGATAACGGGAGCATCTGCATGAGGAT
GGAGATCTTGGGCTGCCCACTGCCGGATCCTAATAACTATTATCACCGACGTAATGAGAT
GACCACCACGGATGACCTGGATTTTAAGCACCACAACTATAAGGAAATGCGCCAGTTGAT
GAAGGTTGTCAATGAAATGTGCCCCAATATTACCAGGATTTACAACATTGGCAAAAGCCA
CCAGGGCCTGAAATTGTATGCGGTAGAGATCTCTGACCATCCTGGGGAACATGAAGTTGG
TGAGCCCGAGTTCCACTACATCGCAGGGGCCCACGGCAATGAGGTTCTGGGACGAGAACT
GCTGCTGCTGCTGCTGCACTTCCTCTGCCAGGAATACTCGGCGCAGAACGCACGCATCGT
CCGCTTGGTGGAGGAGACTCGAATCCACATTCTACCCTCCCTCAATCCTGATGGCTATGA
GAAGGCCTATGAAGGAGGTTCCGAGTTGGGAGGCTGGTCCCTGGGACGTTGGACCCATGA
TGGCATCGATATCAACAACAACTTTCCGGATTTAAACTCGCTGCTCTGGGAGGCAGAGGA
CCAGCAGAATGCCCCAAGGAAGGTCCCCAACCACTACATTGCCATCCCTGAGTGGTTTCT
GTCTGAGAATGCCACAGTGGCCACAGAGACCAGAGCCGTCATCGCCTGGATGGAGAAGAT
CCCGTTTGTGCTGGGAGGCAACCTACAGGGGGGTGAGCTGGTCGTGGCATACCCCTATGA
CATGGTGCGGTCCCTGTGGAAGACCCAGGAGCACACCCCAACACCTGATGATCATGTGTT
CCGCTGGCTGGCGTATTCCTACGCCTCCACTCACCGCCTCATGACAGATGCCAGGAGGCG
AGTGTGCCACACGGAAGATTTTCAGAAGGAGGAGGGCACCGTCAATGGGGCTTCCTGGCA
CACAGTGGCTGGAAGTCTAAACGATTTCAGCTACCTCCATACAAACTGCTTTGAGCTGTC
CATCTACGTGGGCTGTGATAAATACCCACACGAGAGCGAGCTGCCGGAGGAATGGGAGAA
TAACCGGGAGTCTCTGATTGTGTTCATGGAGCAGGTTCATCGAGGCATCAAAGGCATAGT
GAGAGATTTACAAGGGAAAGGGATTTCAAATGCTGTCATCTCTGTGGAAGGTGTTAACCA
TGACATCCGGACAGCCAGCGATGGGGATTACTGGCGTCTACTGAACCCTGGCGAATATGT
GGTCACAGCCAAGGCGGAAGGCTTTATCACTTCCACCAAGAACTGCATGGTTGGCTATGA
TATGGGAGCTACTCGGTGTGACTTCACCCTCACAAAGACCAACCTGGCTAGGATAAGAGA
AATTATGGAGACATTTGGGAAGCAGCCTGTCAGCCTACCCTCCAGGCGCCTGAAGCTGCG
GGGACGGAAAAGGCGGCAGCGTGGGTGACCCTGTCGGACACTTGAGACATACCCCAGACC
GTGCAAATAAAAATCCACTCCAGTAGTAAAAAAA (SEQ ID NO:1)

FIGURE 2A

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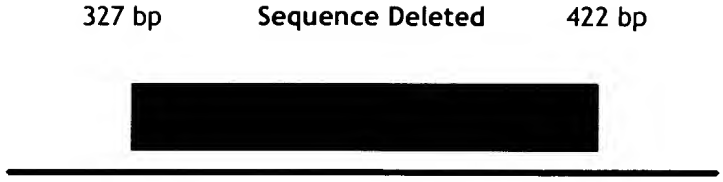
Gene Sequence Structure
*

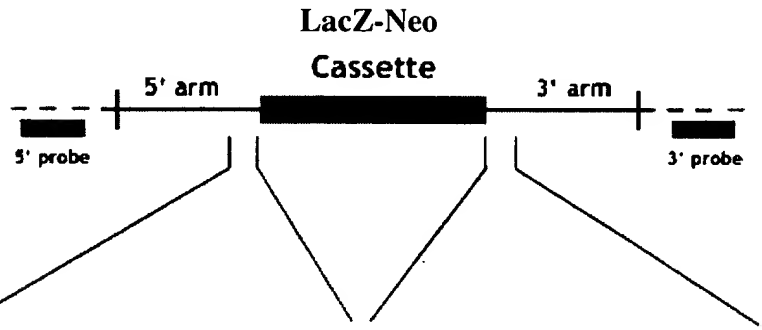
Size of full-length
cDNA: 2490 bp



Targeting Vector*
(genomic sequence)

Construct Number: 2825

Arm Length:
5': 4 kb
3': 1.5 kb



5'>GGCATGGCCCGTCTGGGGACC GCCTGCCCTGCGCTGGCGCTGGCC CTGGCACTTGTGGCGGTGGCCCTG GCTGGAGTCAGAGCCCAGGGCGCA GCCTTCGAGGAGCCTGACTATTAC AGCCAGGAGCTCTGGCGGCGCGGG CGCTATTATGGGCATCCGGAGCCT GAGCCGGAGCCGGAGCTCTTCTCG CCTTCAATGCA<3' (SEQ ID NO:3)	5'>GAGGGAGAAGTTAGTTGCAGA GACGCCTCCACCAGGTAACTTTTG CATCGGGCAGCCCGAGGGGGCGCC AGCGATCGTGGCACTCCAGGGGAC ACCTGGCTTCCAGTATGTTTTCTT GAGTGAGCCCAGCCAAAGTCCTGT GGTGCCTGTGTTATTCCCTAGAGA CTACATCTGAGCTAAGTTCAGCTT TCTCTCCCTGC<3' (SEQ ID NO:4)

Targeting Vector
Endogenous Locus

* Not drawn to scale

FIGURE 2B

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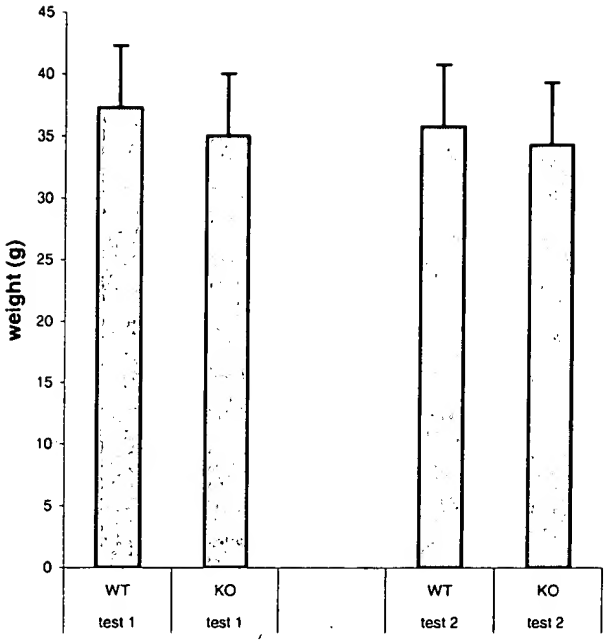

FIGURE 3

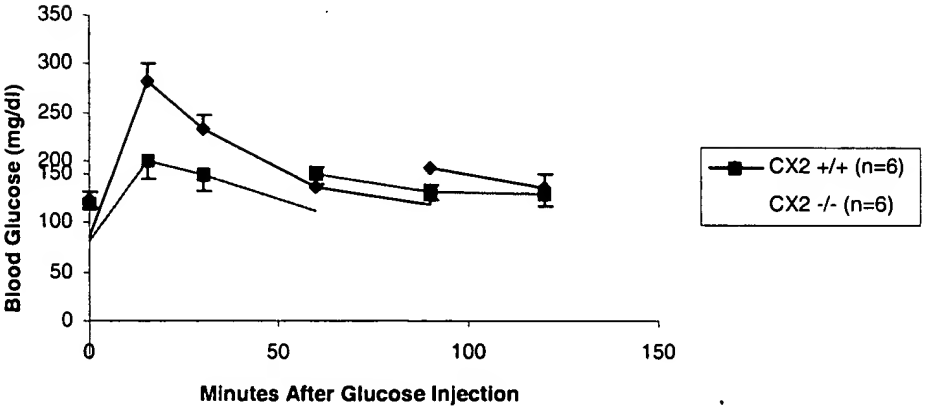

FIGURE 4